CLAIMS

Status of the Claims

Claims 1-31 were originally filed. Claims 4, 6, 10, 14-16 and 21-31 were previously cancelled. Claims 1, 3, 5-13, 17-18, and 20 were previously amended. Herein, Applicant cancels claim 3. Applicant specifically amends and/or cancels all such claims now or previously without prejudice or disclaimer of the subject matter therein and specifically reserves the right to file one or more divisional applications on the amended or cancelled subject matter.

In the Claims

1. (Previously Presented) A method for preparing a protein-polymer conjugate comprising:

(a) contacting an insulin protein in an aqueous solution with an amino-reactive derivative selected from the group consisting of an aldehyde, a N-hydroxy succinimide, a PNP-carbonate, and a benzotrizole terminated hydrophilic polymer of a hydrophilic polymer thereof in the presence of at least one organic solvent selected from the group consisting of ethanol, methanol, DMSO, dioxane, DMF, and NMP and at least one metal chelator selected from the group consisting of metal ion chelators, EDTA, deferoxamine (DEF), diethylenetriamine pentaacetic acid (DTPA), and bis(aminoethyl)glycolether N,N,N',N'-tetraacetic acid (EGTA) to form a conjugate of the protein and the polymer; and

(b) isolating the conjugate.

2. (Original) The method of claim 1, wherein the insulin protein comprises human insulin.

3-4. (Canceled)

5. (Previously Presented) The method of claim 1, wherein the hydrophilic polymer and insulin protein are contacted at a molar ratio of about 10:1-1:1.

6. (Canceled)

7. (Previously Presented) The method of claim 1, wherein the organic solvent is present at a concentration of about 0.1 to 10%.

8. (Previously Presented) The method of claim 1, wherein the insulin protein and hydrophilic polymer are contacted at a protein concentration of about 0.1 -5.0%.

9. (Previously Presented) The method of claim 1, wherein the insulin protein and hydrophilic polymer are contacted at a pH of about 5.0-7.5.

10. (Canceled)

11. (Previously Presented) The method of claim 1, wherein the chelator is present at a concentration of about 0.1-10 mM.

12. (Previously Presented) The method of claim 1, wherein the insulin protein and hydrophilic polymer are contacted at a temperature of about 4-50° C.

13. (Previously Presented) The method of claim 1, wherein the method further comprises the step of quenching formation of the conjugate prior to isolating the conjugate.

14-16. (Canceled)

17. (Previously Presented) The method of claim 1, further comprising the step of encapsulating the conjugate in a biodegradable polymer.

18. (Previously Amended) A method for preparing an insulin-PEG conjugate comprising:

(a) contacting insulin with PEG in an aqueous solution in the presence of at least one organic solvent selected from the group consisting of ethanol, methanol, DMSO, dioxane, DMF, and NMP and at least one metal chelator selected from the group consisting of metal ion chelators, EDTA, deferoxamine (DEF), diethylenetriamine pentaacetic acid (DTPA), and bis(aminoethyl)glycolether N,N,N',N'-tetraacetic acid (EGTA), to form a conjugate of the insulin and PEG; and

(b) isolating the conjugate.

19. (Original) The method of claim 18, wherein the insulin comprises human insulin.

20. (Previously Presented) The method of claim 18, wherein the PEG comprises an amino-reactive PEG derivative selected from the group consisting of an aldehyde, a N-hydroxy succinimide, a PNP-carbonate, and a benzotrizole terminated hydrophilic polymer.

21-31. (Canceled)